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11/18/86

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application Of:

Docket: NRDC-17

DONALD S. ANSON, et al.

Serial Number: 839,215

Group Art Unit: 127

Filed: March 13, 1986

RECEIVED

For: FACTOR IX PROTEIN

NOV 10 1986

GROUP 120

November 5, 1986

INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R.1.97

AND PRELIMINARY AMENDMENT

The Hon. Commissioner of Patents & Trademarks
Washington, D. C. 20231

Sir:

Please amend the specification of this application as follows:

Page 1, line 25, after "EMBO J.," replace "3" by --3,--

Page 2, line 11, replace "amd" by --and--

Page 3, line 24, before "results" replace "The" by --Some--

Page 4, line 5, replace "we" by --were--

Page 4, line 6, replace "decreases" by --decrease--

Page 4, line 31, after "relates" delete "to"

Page 7, lines 4-6, cancel the sentence "In addition, the DNA can include part of the genomic factor IX DNA sequence extending further in the 5'-direction, beyond the precursor-coding region."

Page 8, line 17, cancel the opening bracket

Page 10, line 25, replace "MRNA" by --mRNA--

Page 11, line 2, after "5'---3'," cancel "It" and insert the following new sentence (being the sentence at present at page 11 line 34 to page 12 line 3 with the cancellation of "p5'G/3'" from page 12 line 1):-

a1 --The factor IX DNA insert present in cVI was removed by restriction with BamHI and HindIII and isolated by agarose gel electrophoresis.--

Page 11, line 3, immediately following the above insertion add the following new sentence:-

A1
Centd
--cVI was used in the following stages.--

Page 11, line 3, immediately following the above insertion
begin a new paragraph and insert the following:-

--Separately, to obtain a clone of fully correct factor-
IX cDNA, it--

Page 11, line 34, to page 12, line 3, cancel the sentence:
"The factor IX DNA insert present in p5'G/3' cVI was removed by
restriction with BamHI and HindIII and isolated by agarose gel
electrophoresis."

Page 13, line 16, replace "selective" by --selectable--

Page 15, line 21, after "10" insert "%"

Page 16, line 25, cancel the closing bracket

Page 20, line 21, cancel "p5'G/3'".

Page 25, line 31, cancel the closing bracket.

REMARKS

The above amendments correct minor errors. By way of explanation of the amendments to pages 11 and 20, it has been discovered that the description of the steps leading to the deposited plasmid pIJ5 (see page 20 line 29 - page 21 line 4) were confused with the steps leading to another plasmid. The deposited plasmid contains lacks nucleotides 1-25 and has Nos. 26-40 in inverted order (but still gives the fully active factor IX protein as described). Steps were taken, as described at page 11 lines 3-34, to correct the nucleotide sequence by adding Nos. 1-25 and putting 26-40 the right way round, but the plasmid thus obtained was not that designated pIJ5. While this error is regretted, nothing has been added to or taken away from the overall description of the invention, bearing in mind that the plasmid pIJ5 is of record at an International Depositary Authority pursuant to the Budapest Treaty.

The applicants wish to make of record the references listed on the attached Form PTO-1449. A copy of each such reference is enclosed.

Concise explanation of the relevance of each listed item

The relevance of the following references is described in the specification of the patent application, in the following places:

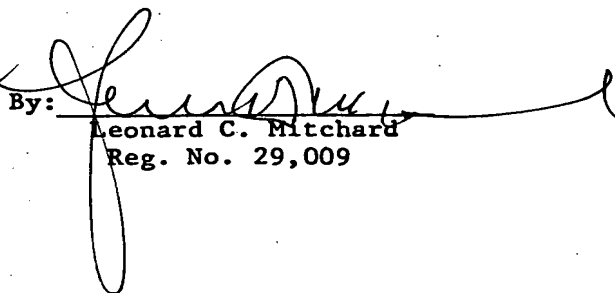
<u>Reference</u>	<u>Description</u>
AL	Page 1 lines 20-26
Note especially page 4 line 25 to page 5 line 28 of this reference, which gives a broad outline of methods of obtaining factor IX protein from the cloned gene.	
AM	Page 2 line 33 to page 3 line 32
AN	Page 3 lines 21-32
(Compare page 48 line 26 - page 49 line 7 of AN with the same page and line portion of AM which are word-for-word identical, although AM is dated 7th May 1985 and AN 9th May 1984).	
AO	Page 3 line 33 to page 4 line 18

AR	Page 1 lines 20 to 26
AS	Page 2 lines 22 to 30
AU	Page 4 lines 19-22
AV	Page 4 lines 23-24
AW	Page 13 lines 5-17
AX	Page 13 lines 18-20
AY	Page 19 lines 12-15

References AM, AN and AO are in the French language. AM and AO should have counterpart U.S. applications, which can no doubt be traced with the aid of the front page information. AN is also in French but is cited only to show identity of a portion of interest with AM and a translation of that portion and its surrounding context (page 49 line 26 to page 50 line 13) is provided herewith.

The following reference (AZ) not mentioned in the specification has been additionally cited and its relevance is as follows. Using a rat hepatoma cell line (H4-11-E-C3, which is the same as is used in Example 1 of the specification) it was shown that the synthesis of the blood clotting factor prothrombin in the cells requires vitamin K to convert preprothrombin to prothrombin. This need not be exogenous vitamin K. The implication is that preprothrombin, which lacks carboxyl chains on its glutamic acid residues, is carboxylated in the cells, since the carboxylation is vitamin K-dependent. (See page 2806, right-hand column, near the top).

Respectfully submitted
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Attachments



11/8/86

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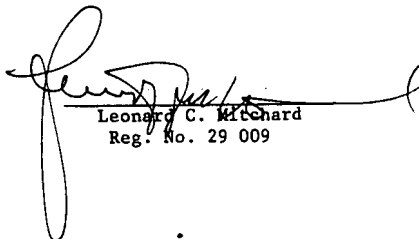
SUBMISSION OF DEPOSIT OF MICROORGANISM PAPERS

The Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

Attached are copies of microorganism deposit papers in connection
with the deposits of strains referred to in the above-identified
application.

Respectfully submitted,
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Attachment - 8 pages